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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/153,133	09/15/1998	D. DUKE LEE	04712/018002	5068

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/153,133	LEE ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 09, 2004 has been entered.

Claims 45-72 are pending. Any rejection that is not addressed in this Office Action is considered obviated in view of the Amendments.

Priority

Priority of the instant application as set forth in Paper No. 6 is September 15, 1998.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. **Claims 45-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,214,368.**

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compositions comprising amorphous calcium phosphate for in vivo use. Accordingly, the scope of the claims overlap.

In the instant case, the patented claims are directed to formable paste composition comprising at least 90% calcium phosphate material and a second calcium phosphate material (see claim 45). The instant claims differ in the amounts of the amorphous calcium phosphate contained within the composition. However, modification of amounts can be achieve by routine experimentation, and the ordinary skill in the art would have had a reasonable expectation to observe beneficial clinical effects of calcium phosphate when administered in vivo.

2. **Claims 45-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,117,456 and claims 1-12 of U.S. Patent 5,683,461.**

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compositions comprising amorphous calcium phosphate for in vivo use. Further both sets of claims only vary in amounts of calcium phosphate concentrations within the claimed compositions. However, it would have been obvious to one of ordinary skill in the art at the time of

invention to optimize such amounts by routine experimentations. Accordingly, the scope of the claims overlap and thus are obvious variants of each other.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

3. Claims 45-46, 48-49, 51-53, 58-61, 63, 72 are rejected under 35 U.S.C. 102(e) as being anticipated by Poser US Patent 5,968,253.

The instant claims are directed to compositions comprising a calcium phosphate source and an active agent wherein the active agent is present in amounts sufficient to elicit a host response protecting the host against a pathogen. The specification at page 7 describes the scope of the term active agent. Accordingly, an active agent is

construed to mean any agent that has biological activity. (see Specification at page 7). Thus, such a term is not viewed to exclude any agent with biological activity.

Poser discloses paste-like flowable compositions comprising 60-95% tricalcium phosphate, a second calcium phosphate source such as monocalcium phosphate monohydrate in a powder form, in combination with an antibiotic and an aqueous injectable lubricant (see abstract, col 6, lines 48-67; col 13, lines 19-51).

Poser's tricalcium phosphate meets the limitation of the instant calcium phosphate. The tricalcium phosphate of Poser is present in dry amount above the 40% by weight of the composition. Such amounts meet solid content of the instantly claimed composition. Poser's monocalcium phosphate monohydrate meets the limitation of the instant adjuvant. The antibiotics employed by Poser falls within the scope of the instant claims, because they are capable to elicit an response against a pathogen in the host. Accordingly, Poser also meets all functional limitations of the instantly claimed composition.

With respect to the method claims Examiner in a claim drawn to a process, the intended use must result in a manipulative difference as compared to the prior art. See *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Here, Poser's method steps is the same as those of the instant claims. Namely, Poser administers a composition, which falls within the scope of the instant claims. (see col 14, lines 55-60). Therefore, there is not manipulative difference between the instant process steps and those of the prior art. Accordingly, method steps of Poser inherently anticipate all functional limitations of the instant claims.

4. Applicant's arguments with respect to this rejection are not found persuasive.

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive. Applicant's interpretation of the scope of the claims is not consistent with the presented arguments. Thus, the arguments are not commensurate with the scope of the claims.

Applicant argues that Poser uses antimicrobials and such agents are excluded from the instant active agents (see Arguments at page 13). In response, Examiner states the generic definitation of active agents at page 7 of the specification does not exclude antimicrobials of Poser.

Applicant further argues that Poser fails to explicitly states that the antimicrobials used by him elicit a host response that protects a host against a pathogen. In response, Examiner states that throughout the prosecution of this Application, all limitations are given their broadest reasonable interpretation consistent with the specification and/or the knowledge in the art. Consistent with such guideline, the phrase "eliciting a host response that protects a host against a pathogen" is viewed to mean any response within the host body that leads to elimination of a pathogen after the active agent is administered into the body.

It is conventional in the art that subsequent to the administration of antibiotics various types of immunological responses leads to activation of cascades or factors; i.e. complement system, chemotaxis, neutrophils, white blood cell, natural killer cells, which ultimately complete the immunological response towards the unwanted pathogen. Such type of immunological responses falls within the scope of the above-mentioned phrase.

Accordingly, antimicrobials recited by Poser anticipate the instant recitation of "active agents."

Finally, Applicant argues that Poser's antimicrobial does not elicit a desired host immune response for purposes of protecting a host. (see Arguments at page 13). As explained throughout the prosecution, Examiner restates that claims 45-46, 48-49, 51-53, 58 are directed to composition of matter. Intended use in such claims is not determinative of the patentability; rather, the central issue is whether all elements of the claimed compositions are described in the compositions of the prior art. Here, the fact that Poser's compositions contain a hapten (i.e. penicillins, sulfonamides, cephelosporins) satisfies the active agent limitation of the instant claims. Therefore, the rejection is proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 45-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poser in view of Classen US Patent 5,723,283 and Reyveld US Patent 4,016,252.

The teachings of Poser are described above. Poser fails to explicitly use a cytokine or an adjuvant for vaccination. Poser also fails to recite the size of is calcium phosphate powder particles.

Classen teaches vaccines for inducing an immunologic response in humans (abstract, col 15-17). Classen teaches the use of various cytokines in combination with an immunogenic agent to enhance the clinical response. (col 17, lines 6-67). Classen describes the use of depot adjuvants such as calcium phosphate salts to prolong the release of immunogenic agent. (see col 20, lines 40-50). Classen also provides for various modes of injectable compositions for use in intravenous, intramuscular or subcutaneous administration. (col 20, lines 56-60; col 52, lines 25-50).

Relyveld teaches the state of art for using calcium phosphate to improve the efficacy of vaccine formulations. The calcium to phosphate ratio in gel formulation of Relyveld is from 1.62 to 1.85 (abstract, col 2 lines 1-15, col 3-4).

The teachings of Poser, Classen and Relyveld are viewed to be in the same field of art, because they all teach various forms of calcium phosphate delivery system.

Even though Poser fails to explicitly use cytokine or adjuvant for vaccination, it would have been obvious to one of ordinary skill in the art at the time of invention to employ a cytokine or immunogenic adjuvant, as described by Classen, to improve the clinical efficacy of the drug delivery systems of Poser.

Further, since using a bioactive agent are art recognized equivalents for the purposes of incorporation into a calcium phosphate delivery system, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute or employ anyone of the immunogens described in Classen, in Poser's composition.

Finally, absence of showing unexpected results, optimizing the particle sizes of Poser's compositions for the optimal clinical effects would have been well within the level of one of ordinary skill in the art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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